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AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Oncology* (*WJGO*, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc*.

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ORIGINAL ARTICLE

Retrospective Study

Should we perform sigmoidoscopy for colorectal cancer screening in people under 45 years?

Waiian Leong, Jia-Qi Guo, Chun Ning, Fei-Fei Luo, Rui Jiao, Dong-Ye Yang

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Abstract

BACKGROUND

The strategy for preventing colorectal cancer is screening by colonoscopy, which offers a direct way for detection and removal of adenomatous polyps (APs). American College of Gastroenterology guidelines recommend that people aged ≥ 45 years should undergo colonoscopy; however, how to deal with people aged ≤ 45 years is still unknown.

AIM

To compare the prevalence of APs and high-grade neoplasia between the left and right colon in patients ≤ 45 years.

METHODS

A retrospective observational study was conducted at a single tertiary III hospital in China. This study included patients aged 18–45 years with undergoing initial colonoscopy dissection and pathological diagnosis AP or high-grade neoplasia between February 2014 and January 2021. The number of APs in the entire colon while screening and post-polypectomy surveillance in following 1–3 years were evaluated.

RESULTS

A total of 3053 cases were included. The prevalence of APs in the left and right colon was 55.0% and 41.6%, respectively (OR 1.7, 95%CI 1.6–2.4; $P < 0.05$). For APs with high-grade neoplasia, the prevalence was 2.7% and 0.9%, respectively (OR 3.0, 95%CI 2.0–4.6; $P < 0.05$). Therefore, the prevalence of APs and high-grade neoplasia in the left colon was significantly higher than in the right colon in patients aged ≤ 45 years. There were 327 patients who voluntarily participated in post-polypectomy surveillance in following 1–3 years, and APs were found in 216 cases (66.1%); 170 cases had 1–3 polyps (52.0%) and 46 cases had > 3 polyps (14.1%; OR 0.3, 95%CI 0.1–0.6; $P < 0.05$).

CONCLUSION

This study suggests that flexible sigmoidoscopy would be an optimal approach for initial screening in people aged ≤ 45 years and would be a more cost-effective and safe strategy.

Key Words: Adenomatous polyps; High-grade neoplasia; Colonoscopy; Flexible sigmoidoscopy

Core Tip: This was a retrospective observational study to investigate the prevalence of adenomatous polyps (APs) and high-grade neoplasia and establish the significant difference between the left and right colon in patients aged ≤ 45 years. The prevalence of APs and high-grade neoplasia in the left colon was significantly higher than that in the right colon. This suggests that flexible sigmoidoscopy would be an optimal approach for the initial screening in people aged ≤ 45 years and would be a more cost-effective and safe strategy. Colonoscopy for post-polypectomy surveillance could be conducted at an appropriate interval of approximately 3 years.

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INTRODUCTION

Colorectal cancer (CRC) is not only the third most common cancer but also the third cause of cancer mortality worldwide, with > 1.85 million cases and > 850000 deaths annually[1]. The incidence of CRC is increasing in both developed and developing regions and countries since the lifestyle of more people, especially young people, shifts toward a western high-fat and high-calorie diet with less exercise, and obesity and metabolic syndrome are prevalent[2,3]. Several studies have indicated that the incidence of CRCs at age < 50 years has been increasing in recent years[4,5]. About 70% of sporadic CRCs developing from adenomatous polyps (APs) through the adenoma–carcinoma sequence[6,7]. New American College of Gastroenterology (ACG) guidelines suggest CRC screening in average-risk individuals aged ≥ 45 years to reduce the incidence of advanced adenoma and CRC, and mortality from CRC[8].

Colonoscopy with pathological examination is considered the most effective strategy for CRC screening because it can directly remove polyps and achieve pathological diagnosis of adenoma, high-grade neoplasia, or early-stage CRC. However, colonoscopy needs experienced doctors, sedation or anesthesia, good bowel preparation and longer examination time. Also, it may increase medical consumption, the potential for patient discomfort and the risk of complications[9,10].

Since the new ACG guideline recommended coloscopy screening in people aged ≥ 45 years, how to deal with those ≤ 45 years is still debatable, and whether they need colonoscopy screening is unknown. Our study aimed to compare the prevalence of APs and high-grade neoplasia between the left colon (including rectal, sigmoid, descending colon and spleen flexure) and right colon (including transverse, ascending, hepatic flexure, cecum, and ileocecal) in patients aged ≤ 45 years visiting our outpatient clinic, to identify whether flexible sigmoidoscopy would be an optimal approach for their initial CRC screening. In addition, the numbers of APs in the entire colon detected by post-polypectomy surveillance in the following 1–3 years were evaluated to provide an appropriate interval for follow-up.

MATERIALS AND METHODS

Study design

To retrospectively evaluate the distribution of APs and compare the prevalence of neoplasia in the left and right colon of patients in the outpatient clinic at the University of Hongkong-Shenzhen Hospital, a tertiary III hospital located in southern China. The data were collected from our endoscope center and pathology department spanning from February 2014 to January 2021. All colonoscopies were performed by experienced endoscopists with the time of coloscopy pull-out

time over 9 min and adequate bowel cleanliness which Boston Bowel Preparation Scale > 6 in all three segments, as well as the ability to detect polyps ≥ 5 mm in size[11,12]. Tissue specimens were evaluated by two gastrointestinal pathologists. The histopathological diagnosis was based on the morphological features on hematoxylin and eosin staining.

Participant selection and data collection

All patients (aged 18–45 years) underwent initial colonoscopy as opportunistic examination according to specialist's medical recommendation for assessment of gastrointestinal symptoms, or patient initiative rather than CRC screening according to guidelines from 1 February 2014 to 31 January 2021 in our hospital. Their pathological diagnosis included polypoid mucosa, inflammatory polyps (pseudopolyp), hyperplastic polyps, sessile serrated polyps, APs, and APs with high-grade neoplasia. A total of 3053 independent cases were included (colonoscopies at intervals of ≤ 6 months were considered as the same cases for our purposes). The exclusion criteria were patients aged < 18 years or > 45 years; or histopathological diagnosis of CRC. A retrospective chart review of electronic medical records and electronic colonoscopy and histopathological reports was performed to collect data on patient demographics, colonoscopy and colonic location, and pathological classification of all polyps were recorded.

Study outcome and definitions

The study outcome was the prevalence of APs in the left and right colon. Polypoid mucosa, inflammatory polyps, and hyperplastic polyps were defined as non-APs. In addition, APs with high-grade neoplasia included polyps with high-grade intraepithelial tumor and high-grade dysplasia. The term left colon included the rectum, sigmoid, descending colon, and splenic flexure, and the right colon included the transverse colon, ascending colon, hepatic flexure, cecum and ileocecal region. Our primary analysis focused on the rates of APs between the left and right colon. We also studied patients after follow-up of 1–3 years for post-polypectomy surveillance. The recurrence of APs was measured during follow-up.

Statistical analysis

All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc, Cary, NC, United States) and GraphPad Prism 8 (GraphPad, San Diego, CA, United States). Categorical variables are summarized as percentages, and continuous variables are summarized as means ± SD. Between group comparisons were evaluated using the χ^2 test or Fisher's exact test, and estimated OR, and 95%CI. Two-sided $P \leq 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics

A total of 66008 cases underwent colonoscopy from 1 February 2014 to 31 January 2021 in our hospital; and 31485 cases (47.7%) underwent colonoscopy aged ≤ 45 years. There were 3265 cases (2747 patients) with histological diagnosis of noncancerous lesions and 3053 cases as independent cases were included for final analysis; of which 2138 cases were male (70%) with an average age of 38.33 ± 5.15 years. For histopathological diagnosis in the entire colon, 2652 cases (86.9%) were APs and 106 cases (3.5%) were APs with high-grade neoplasia. In addition, there were 19 cases with both APs and high-grade neoplasia in the entire colon. There were 314 cases of non-APs. The demographic characteristics are shown in Table 1.

Prevalence and distribution of adenomatous polyps

To assess the characteristics of APs, we analyzed the relation between the position in the colon. The cases of APs in the left, right and both sides of the colon was 1679, 1271 and 298, respectively. The prevalence in the left and right colon was 55% and 41.6%, respectively (OR 1.7, 95%CI 1.6–2.4; $P < 0.05$). For APs with high-grade neoplasia, there were 82, 28 and 4 in the left, right and both sides of the colon, respectively. The prevalence in the left and right colon was 2.7% and 0.9%, respectively (OR 3.0, 95%CI 2.0–4.6; $P < 0.05$). Compared to the right colon, APs and APs with high-grade neoplasia in the left colon were significantly higher (Table 2 and Supplementary Table 1). Surprisingly, similar results were found in patients aged < 40 years, which included 1659 cases (1400 patients), but there was no significant difference between ≤ 45 years and < 40 years either left colon or entire colon (Supplementary Table 2).

Post-polypectomy surveillance after screening

For post-polypectomy surveillance, 430 cases (14.1%, 346 participants) were followed up with two or more colonoscopies at intervals > 6 months, and 327 cases (76.1%, 282 participants) were followed up for 1-3 years. There were 216 cases (66.1%) of APs and 111 cases (33.9%) non-APs in the entire colon. For APs, there were 170 cases with 1–3 polyps (52.0%) and 46 cases with > 3 polyps (14.1%). In addition, among non-APs, 104 cases had 1–3 polyps (31.8%) and 7 cases had > 3 polyps (2.1%; OR 0.3, 95%CI 0.1–0.6; $P < 0.05$; Table 3).

DISCUSSION

CRC remains common worldwide and an important public health concern. With a steadily increasing incidence and mortality associated with CRC in adults younger than 50 years, the guideline update recommends that individuals aged ≥

Table 1 Baseline characteristics of the study participants

Characteristics	All independent cases for research, *n* = 3053	Adenomatous polyps, *n* = 2652	Adenomatous polyps with high-grade neoplasia *n* = 106
Age (yr, mean ± SD)	38.33 ± 5.15	38.41 ± 5.08	37.28 ± 5.51
Sex [*n* (%)]			
Male	2138 (70.0)	1842 (69.5)	72 (67.9)
Female	915 (30.0)	810 (30.5)	34 (32.1)

Table 2 The prevalence of adenomatous polyps in the left and right colon

	Entire colon	Both left-and right colon	Left colon	Right colon	OR (95%CI) of left *vs* right colon	*P* value of left *vs* right colon
Adenomatous polyps [*n* (%)]	2652 (86.9)	298 (0.9)	1679 (55.0)	1271 (41.6)	1.7 (1.6-2.4)	0.0001
Adenomatous polyps with high-grade neoplasia [*n* (%)]	106 (3.5)	4 (0.1)	82 (2.7)	28 (0.9)	3.0 (2.0-4.6)	0.0001

Table 3 The adenomatous polyps in entire colon for screening and post-polypectomy surveillance in the following 1–3 yr

The numbers of polyps in follow-up cases, *n* = 327	Adenomatous polyps, *n* = 216	Non-adenomatous Polyps, *n* = 111	OR (95%CI)	*P* value
1-3 polyps [*n* (%)]	170 (52.0)	104 (31.8)	0.3 (0.1-0.6)	0.0004
> 3 polyps [*n* (%)]	46 (14.1)	7 (2.1)		

45 years with an average risk of CRC undergo tailored screening[8,13,14]. To our knowledge, none of the studies have shown the screening recommendations and strategies for individuals aged ≤ 45 years. Our study showed that the prevalence of APs in the left colon was significantly higher than in the right colon, whether or not with high-grade neoplasia, and recurrence of > 3 APs was < 15% during 1–3 years follow-up. The results suggest that sigmoidoscopy for primary screening would be a potential approach and colonoscopy for post-polypectomy surveillance would be intervals around 3 years in people aged ≤ 45 years. This would be a more cost-effective, less risky strategy for CRC screening in that age group.

Early onset CRC (EOCRC), diagnosed at aged < 50 years, is a heterogeneous disease and almost two-thirds of cases occur between the ages of 40 and 49 years[5,15]. Recent data from SEER (Surveillance, Epidemiology, and End Results) and National Program of Cancer Registries databases found that approximately 42% of tumors were in the rectum[16]. Most cases of EOCRC are identified through screening because of high-risk and red flag symptoms such as anemia without apparent cause, hematochezia, change in bowel habits, and abdominal pain; thus, these cases tend to have a longer duration to diagnosis than those from people aged > 50 years[17-19]. APs are the precursors for aggressive CRCs and 60%–70% of sporadic CRCs develop from APs through the adenoma–carcinoma pathway *via* a multistep over several years or even a decade[6,7,20,21]. Early detection and resection of precancerous polyps are critical to interrupt the adenoma–carcinoma process, preventing the development of CRC. However, given the EOCRC characteristics, Laiyemo and Pinsky[22] also suggested that widespread use of colonoscopy among young persons may be leading to over detection and insurance consumption in the United States.

Accordingly, CRC screening has contributed to reduction of CRC-related morbidity and mortality through the detection and removal of APs and other precancerous lesions, but clinicians have to weigh against the benefits, risks, costs and insurance burden. CRC screening includes colonoscopy, flexible sigmoidoscopy (FS), computed tomography colonography (CTC), colon capsule endoscopy (CCE), fecal immunochemical test, multitarget stool DNA test, and blood septin 9; each of which has advantages and limitations[8,14]. The first four involve structural examination that allows the operator a visual inspection of the bowel. CTC and CCE, despite being noninvasive screening and emerging technologies, require follow-up with timely colonoscopy for further evaluation or biopsy if there is a positive test result[9,23]. Moreover, CTC is not good at detection of flat adenomatous or serrated polyps, due to its dependence on morphology as well as the need for full bowel cleansing preparation and radiation exposure. There is no empirical evidence to demonstrate that CTC can reduce CRC incidence or related mortality[9,12]. On the contrary, colonoscopy and FS, although invasive, offer the optimize direct detection of precancerous lesions as well as simultaneous removal of lesions, which provide long-term protection against CRC morbidity and mortality[10,24]. However, colonoscopy requires better adequate bowel preparation and the adenoma detection rate is positively correlated with the quality of cleansing and the withdrawal time. Additionally, it needs experienced endoscopists who are well trained, and is better under conscious sedation or anesthesia, which has a risk of complications and incurs higher costs[12,23,25,26]. FS reaches the splenic

flexure or approximately 60 cm from the anal dentate line with less invasion and lower risk of complications, has > 95% sensitivity for CRCs and > 70% sensitivity for APs, which are the same as distal colonoscopy[27,28]. Besides, the advantages of FS are the need for less time for preoperative preparation and lower cost without any sedation or anesthesia[29,30]. In four large randomized controlled trials with 11–17 years of follow-up, the intention-to-treat analysis reported a 27% reduction in the incidence of CRC and a 21% reduction in mortality; moreover, the per-protocol analyses reported 31%–33% reduction in the incidence and 38%–43% reduction in mortality with screening by FS[31-34]. Furthermore, recent studies demonstrated that the effect of FS is similar to colonoscopy in the distal colon[9,35]. Compared with the right colon, there were a 1.7-fold increase in APs and threefold increase in APs with high-grade neoplasia in the left (Table 2). Our findings are consistent with prior studies in the SEER national database that reported that incidence of EOCRC tends to more often present in the left colon or in the rectum[36].

Given that the incidence of EOCRC is showing an alarming increase, the 2018 American Cancer Society and 2021 ACG guidelines recommend lowering the CRC screening initiation age from 50 to 45 years to reduce subsequent CRC incidence and improve cost-effectiveness[8,13]. Some research has suggested initiating screening at aged 40 years[36,37]. In our study, there were no significant differences between patients aged ≤ 45 years and < 40 years for prevalence of APs or APs with high-grade neoplasia in the left colon or entire colon. Hence, these results imply that lowering the age to 40 years would not provide more benefit than age ≤ 45 years (Supplementary Table 2).

Several societies and organizations have issued surveillance guidelines for patients who are undergoing screening or post-polypectomy surveillance. The current guidelines suggest that FS should be repeated every 5 years in asymptomatic individuals with no previous history of polyps[14,38]. After positive findings, repeated colonoscopy and frequent surveillance are recommended. The majority of people with polypectomy would receive surveillance colonoscopy every 1, 3, 5 or 10 years depending on the polyp characteristics, including size, number and histological features[8,25]. According to risk stratification for colorectal APs, the regular surveillance intervals are recommended every 3–5 years for patients with high-risk and every 5–10 years patients with low risk[13,25]. In our cohort, we found that recurrent APs were found in approximately 10% of patients with follow-up screening or postresection surveillance after 1–3 years. Among them, approximately two thirds had APs in the entire colon; moreover, there was lower recurrence of > 3 APs compared with 1–3 polyps (14% *vs* 52.0%; Table 3). Therefore, we suggest that colonoscopy for postresection surveillance would be adequate at longer intervals of approximately 3 years to reduce invasiveness and improve cost-effectiveness.

There were some limitations to our study. First, this was a single center, retrospective observational study which was prone to selection bias. Second, our study did not show any correlation between smoking, moderate alcohol consumption, obesity, red meats, processed meats, and diabetes/metabolic syndrome, which are considered high-risk factors for EOCRC, as well as family history of CRC and polyps because it was not CRC screening in average-risk individuals[2,19]. Additionally, the presence or absence of symptoms such as pain, bleeding, or altered bowel habits was not recorded[19]. Third, although all endoscopists met the eligibility requirements for endoscopic procedures, they were randomly arranged irrespective of their experience. This could have led to underestimation of the true prevalence. Finally, the post-polypectomy surveillance period depended on the patients' preference, including gastrointestinal symptoms or individual willing. Moreover, due to insurance status, financial motivations, and personal or working reasons to move out of the city of Shenzhen, some patients would choose other hospitals or were lost to follow-up, which could have influenced the outcome of postresection follow-up.

CONCLUSION

This retrospective study suggests that FS would be an optimal primary approach for CRC screening in people aged ≤ 45 years; and post-polypectomy surveillance could be performed at an appropriate interval of approximately 3 years. However, there is still a need for prospective, multicenter research for confirmation.

ARTICLE HIGHLIGHTS

Research background

Early onset colorectal cancer (CRC) has shown a steadily increasing incidence and mortality such that the updated guidelines recommend individuals aged ≥ 45 years with an average-risk of CRC undergo screening. However, whether people aged ≤ 45 years need colonoscopy screening or other tailored screening is unknown.

Research motivation

What is the better approach of CRC screening for people aged ≤ 45 years.

Research objectives

This study aimed to investigate the prevalence of adenomatous polyps (AP) and high-grade neoplasia as well as compare and find out the significant difference between the left- and right- colon in patients under 45 years.

Research methods

A retrospective observational study was conducted in patients aged 18–45 years who underwent initial colonoscopy from

February 2014 to January 2021 at a tertiary III hospital in China.

Research results

The prevalence of both APs and high-grade neoplasia in the left colon was significantly higher than in the right colon in people aged ≤ 45 years. The recurrence of > 3 APs was < 15% after 1–3 years follow-up.

Research conclusions

Flexible sigmoidoscopy would be an optimal approach for the initial screening in people aged ≤ 45 years and would be a more cost-effective and safe strategy.

Research perspectives

Further multicenter, large clinical and prospective studies are still needed to verify the results of the present study and investigate CRC in average-risk individuals aged ≤ 45 years.

FOOTNOTES

Author contributions: Leong W and Yang D designed and performed the research and wrote the paper; Guo J and Ning C contributed to collect data; Leong W and Ning C contributed to analysis data; Lo F and Jiao R provided clinical advice; Yang D supervised the report.

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Institutional review board statement: The need for ethics committee or institutional review board approval was not necessary because this manuscript is a retrospective observational study that is not involved any genetic testing clinical trials and unconventional clinical practice or treatments. The analysis used anonymous clinical data.

Informed consent statement: In this retrospective observational study, patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: The authors declare that there is no conflict of interests.

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